

*SUB B3 cont* → FISYDGSNKHYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO: 37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively.

Please replace the paragraph beginning on page 7, line 13, with the following amended paragraph:

*SUB B3* → Other human sequence antibodies of the invention comprise heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively.

Please replace the paragraph beginning on page 8, line 3, with the following amended paragraph:

*SUB B3* → The invention provides a hybridoma cell line comprising a B cell obtained from a transgenic non-human animal having a genome comprising a human sequence heavy chain transgene and a human sequence light chain transgene, wherein the hybridoma produces a human sequence antibody that specifically binds to human CTLA-4. In a related embodiment, the hybridoma secretes a human sequence antibody that specifically binds human CTLA-4 or binding fragment thereof, wherein the antibody is selected from the group consisting of: a human sequence antibody comprising heavy chain heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGNNKYYADSVKG (SEQ ID NO:32) and TGWLGPFDY (SEQ ID NO:37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVGSSYLA (SEQ ID NO:24), GAFSRAT (SEQ ID NO:29), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:17 and SEQ ID NO:7, respectively; a human sequence antibody comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHYADSVKG

and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 23, with the following amended paragraph:

The gamma1 heavy chain plasmid, pCG7-96 (SEQ ID NO:40), includes the human gamma1 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pCG7-96 digested with HindIII and AgeI to reconstruct a complete gamma1 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/SalI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 31, with the following amended paragraph:

The gamma4 heavy chain plasmid, pG4HE (SEQ ID NO:41), includes the human gamma4 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pG4HE digested with HindIII and AgeI to reconstruct a complete gamma4 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/EcoRI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please insert the following paragraph immediately before the paragraph beginning at page 93, line 1 of the specification:

SEQ ID NO:1 pGP1k

AATTAGCGGC CGCTGTCGAC AAGCTTCGAA TTCAGTATCG ATGTGGGGTA      50  
CCTACTGTCC CGGGATTGCG GATCCGGAT GATATCGTTG ATCCTCGAGT      100  
GCGGCCGAG TATGCAAAAA AAAGCCCCCT CATTAGGCGG GCTCTTGGCA      150  
GAACATATCC ATCGCGTCCG CCATCTCCAG CAGCCGCACG CGGCCGCATCT      200  
CGGGCAGCGT TGGGTCTGG CCACGGGTGC GCATGATCGT GCTCCTGTCG      250

GTTCCGCGCA CATTCCCCG AAAAGTGCCA CCTGACGTCT AAGAAACCAT 3100  
TATTATCATG ACATTAACCT ATAAAAATAG GCGTATCACG AGGCCCTTC 3150  
GTCTTCAAG 3159

Please replace the paragraph beginning on page 93, line 1, with the following amended paragraph:

pCK7-96 (Nucleotide residues 3376 to 3881)(SEQ ID NO:39)

AGGAGAATGAATAAATAAAGTGAATCTTCACCTGTGGTTCTCTCTTCCCAATTAAATTATT  
ATCTGTTGTTACCAACTACTCAATTCTCTTATAAGGGACTAAATATGTAGTCATCCTAAGGCGCATA  
ACCATTATAAAAATCATCCTCATTCTATTCTACCTATCATTCTGCAGACAGTCCTCCCTCAA  
CCCACAAGCCTCTGCTCACAGTCCCCTGGCCATGGATCCTCACATCCCAATCCGGCCGCAATT  
CGTAATCATGGTCATAGCTGTTCTGTGTGAATTGTTATCCGCTCACAAATTCCACACAACATACGAG  
CCGGAAGCATAAAGTGTAAAGCCTGGGTGCCTAATGAGTGAGCTAACATTAATTGCGTTGCGCT  
CACTGCCGCTTCCAGTCGGAAACCTGTCGTGCCAGCTGCATTAAATGAATCGGCCAACGCGCGGGGA  
GAGGCGGTTGCGTATTGGGC

Please replace the paragraph beginning on page 93, line 8, with the following amended paragraph:

pCG7-96 (SEQ ID NO:40)

Please replace the paragraph beginning on page 94, line 12, with the following amended paragraph:

pG4HE (SEQ ID NO:41)

Please replace the paragraph beginning on page 95, line 17, with the following amended paragraph:

10D1 VH(SEQ ID NO:16)

Please replace the paragraph beginning on page 95, line 27, with the following amended paragraph:

10D1 VK(SEQ ID NO:6)

Please replace the paragraph beginning on page 95, line 37, with the following amended paragraph:

4B6 VH(SEQ ID NO:18)

The following new paragraph has been inserted immediately before the paragraph beginning on page 93, line 1, of the specification:

SEQ ID NO:1 pGP1k

AATTAGCGGC CGCTGTCGAC AAGCTTCGAA TTCAGTATCG ATGTGGGTA	50
CCTACTGTCC CGGGATTGCG GATCCCGCAT GATACTGTTG ATCCTCGAGT	100
GCGGCCGCAAG TATGCAAAAAA AAAGCCCGCT CATTAGGCCG GCTCTTGGCA	150
GAACATATCC ATCGCGTCCG CCATCTCCAG CAGCCGCACG CGGCGCATCT	200
CGGGCAGCGT TGGGTCTTGG CCACGGGTGC GCATGATCGT GCTCCTGTG	250
TTGAGGACCC GGCTAGGCTG GCGGGGTTGC CTTACTGGTT AGCAGAACG	300
ATCACCGATA CGCGAGCGAA CGTGAAGCGA CTGCTGCTGC AAAACGCTG	350
CGACCTGAGC AACAAACATGA ATGGTCTTCG GTTTCCGTGT TTGTAAGT	400
CTGAAACCGC GGAAGTCAGC GCCCTGCACC ATTATGTTCC GGATCTGCAT	450
CGCAGGATGC TGCTGGCTAC CCTGTGGAAC ACCTACATCT GTATTAACGA	500
AGCGCTGGCA TTGACCCCTGA GTGATTTTC TCTGGTCCCCG CGCATCCAT	550
ACCGCCAGTT GTTTACCCCTC ACAACGTTCC AGTAACCGGG CATGTTCATC	600
ATCAGTAACC CGTATCGTGA GCATCCTCTC TCGTTTCATC GGTATCATTA	650
CCCCCATGAA CAGAAAATTCC CCCTTACACG GAGGCATCAA GTGACCAAAC	700
AGGAAAAAAC CGCCCTTAAC ATGGCCCGCT TTATCAGAAC CGAGACATTA	750
ACGCTCTGG AGAAACTCAA CGAGCTGGAC GCGGAATGAAAC AGGCAGACAT	800
CTGTGAATCG CTTCACGACC ACGCTGATGA GCTTTACCCG AGCTGCCTG	850
CGCGTTTCGG TGATGACGGT GAAAACCTCT GACACATGCA GCTCCCGGAG	900
ACGGTCACAG CTTGTCTGTA AGCGGATGCC GGGAGCAGAC AAGCCCGTCA	950
GGGCGCGTCA CGGGGTGTTG CGGGGTGTCG GGGCGCAGCC ATGACCCAGT	1000
CACGTAGCGA TAGCGGAGTG TATACTGGCT TAACTATGCG GCATCAGAGC	1050
AGATTGTACT GAGAGTGCAC CATATGCCGT GTGAAATACC GCACAGATGC	1100
GTAAGGAGAA AATACCGCAT CAGGCCCTCT TCCGCTTCCT CGCTCACTGA	1150
CTCGCTGCGC TCGGTGTTG GGCTGCGCG AGCGGTATCA GCTCACTCAA	1200
AGGCGGTAAT ACGGTTATCC ACAGAACATCG GGGATAACGC AGGAAAGAAC	1250
ATGTGAGCAA AAGGCCAGCA AAAGGCCAGG AACCGTAAAA AGGCCCGTT	1300
GCTGGCGTT TTCCATAGGC TCCGCCCCCC TGACGAGCAT CACAAAAATC	1350
GACGCTCAAG TCAGAGGTGG CGAAACCCGA CAGGACTATA AAGATACCAG	1400
GCGTTCCCC CTGGAAGCTC CCTCGTGCCTC TCTCCTGTT CGACCCCTGCC	1450
GCTTACCGGA TACCTGTCCG CCTTTCTCCC TTCCGGAAAGC GTGGCGCTTT	1500
CTCATAGCTC ACGCTGTAGG TATCTCAGTT CGGTGTAGGT CGTTCGCTCC	1550
AAGCTGGCT GTGTGCACGA ACCCCCCGTT CAGCCCGACC GCTGCGCCTT	1600
ATCCGGTAAC TATCGTCTTG AGTCCAACCC GGTAAAGACAC GACTTATCGC	1650
CACTGGCAGC AGCCAGGCAGC GCCTTGGCCT AAGAGGCCAC TGGTAACAGG	1700
ATTAGCAGAG CGAGGTATGT AGGCGGTGCT ACAGAGTTCT TGAAGTGGTG	1750
GCCTAACTAC GGCTACACTA GAAGGACAGT ATTGGTATC TGCGCTCTGC	1800
TGAAGCCAGT TACCTTCGGA AAAAGAGTTG GTAGCTCTG ATCCGGCAAA	1850
CAAACCACCG CTGGTAGCGG TGGTTTTTT GTTGCAAGC AGCAGATTAC	1900
GCGCAGAAAA AAAGGATCTC AAGAAGATCC TTTGATCTT TCTACGGGTT	1950
CTGACGCTCA GTGGAACGAA AACTCACGTT AAGGGATTG GGTACATGAGA	2000
TTATCAAAAA GGATCTTCAC CTAGATCCTT TAAATTAAT AATGAAGTTT	2050
TAATCAATC TAAAGTATAT ATGAGTAAAC TTGGTCTGAC AGTTACCAAT	2100
GCTTAATCAG TGAGGCACCT ATCTCAGCGA TCTGTCTATT TCGTTCATCC	2150
ATAGTTGCCT GACTCCCCGT CGTGTAGATA ACTACGATAC GGGAGGGCTT	2200
ACCATCTGGC CCCAGTGCTG CAATGATACC GCGAGACCCA CGCTCACCGG	2250
CTCCAGATT ATCAGCAATA AACCAAGCCAG CGGAAAGGGC CGAGCGCAGA	2300
AGTGGTCCCTG CAACTTATC CGCCTCCATC CAGTCTATT ATTGTTGCCG	2350
GGAAGCTAGA GTAAGTAGTT CGCCAGTTAA TAGTTGCAG AACGTTGTTG	2400
CCATTGCTGC AGGCATCGTG GTGTCACGCT CGTCGTTGG TATGGCTTCA	2450
TTCAAGCGA GTTACATGAT CCCCCATGTT	2500

GTGCAAAAAA GCGGTTAGCT CCTTCGGTCC TCCGATCGTT GTCAGAAAGTA 2550  
AGTTGGCCGC AGTGTATCA CTCATGGTTA TGCGACACT GCATAATTCT 2600  
CTTACTGTCA TGCCATCCGT AAGATGCTTT TCTGTGACTG GTGAGTACTC 2650  
AACCAAGTCA TTCTGAGAAT AGTGTATGCG GCGACCGAGT TGCTCTGCC 2700  
CGGCGTCAAC ACAGGGATAAT ACCCGGCCAC ATAGCAGAAC TTAAAAGTG 2750  
CTCATCATTG GAAAACGTT TCAGGGCGA AAACCTCTCAA GGATCTTACC 2800  
GCTGTTGAGA TCCAGTCGA TGTAACCCAC TCGTGCACCC AACTGATCTT 2850  
CAGCATCTT TACTTCACC AGCGTTCTG GGTGAGCAAA AACAGGAAGG 2900  
CAAAATGCCG CAAAAAAGGG AATAAGGGCG ACACGGAAAT GTTGAATACT 2950  
CATACTCTTC CTTTTCAAT ATTATTGAAG CATTATCACG GGTATTTGTC 3000  
TCATGAGCGG ATACATATTT GAATGTATTT AGAAAAATAA ACAAATAGGG 3050  
GTTCCGCGCA CATTCCCCG AAAAGTGCCA CCTGACGTCT AAGAAACCAT 3100  
TATTATCATG ACATTAACCT ATAAAATAG GCGTATCACG AGGCCCTTTC 3150  
GTCTTCAAG 3159

The paragraph beginning on page 93, line 1, has been amended as follows:

**pCK7-96 (Nucleotide residues 3376 to 3881)(SEQ ID NO:39)**

AGGAGAAATGAATAATAAAAGTGAATCTTGACCTGTGGTTCTCTCTTCAATTAAATAATTATT  
ATCTGTTGTTACCAACTACTCAATTCTTATAAGGGACTAAATATGTAGTCATCCTAAGGCGCATA  
ACCATTATAAAAATCATCCTTCATTCTATTTACCCATCATCCTCTGCAAGACAGTCCTCCCTCAAA  
CCCACAAGCCTCTGCTCTCACAGTCCCCTGGGCATGGATCCTCACATCCCAATCCGCGGCCGCAATT  
CGTAATCATGGTCATAGCTTTCTGTGAAATTGTTATCCGCTCACATTCCACACAACATACGAG  
CCGGAAGCATAAAGTGTAAAGCCTGGGGCTAACATGAGTGAGCTAACTCACATTAATTGCGTTGCGCT  
CACTGCCCCCTTCCAGTCGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGCCAACGCGCGGGGA  
GAGGCGGTTGCGTATTGGGGCG

The paragraph beginning on page 93, line 8, has been amended as follows:

**pCG7-96 (SEQ ID NO:[41]40)**

The paragraph beginning on page 94, line 12, has been amended as follows:

**pG4HE (SEQ ID NO:[42]41)**

The paragraph beginning on page 95, line 17, has been amended as follows:

**10D1 VH(SEQ ID NO:16)**

The paragraph beginning on page 95, line 27, has been amended as follows:

**10D1 VK(SEQ ID NO:6)**

The paragraph beginning on page 95, line 37, has been amended as follows:

**4B6 VH(SEQ ID NO:18)**

The paragraph beginning on page 95, line 47, has been amended as follows:

**4B6 VK(SEQ ID NO:8)**

The paragraph beginning on page 95, line 57, has been amended as follows:

**1E2 VH(SEQ ID NO:22)**

The paragraph beginning on page 96, line 7, has been amended as follows:

**1E2 VK(SEQ ID NO:12)**

**IN THE CLAIMS:**

31. (Amended) The human sequence antibody of claim 1, comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO:[38]37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively.

32. (Amended) The human sequence antibody of claim 1, comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ